Comorbidity burden is associated with poor psychological well-being and physical health status in patients with an implantable cardioverter-defibrillator

Hoogwegt, M.T.; Kupper, N.; Jordaens, L.; Pedersen, S.S.; Theuns, D.A.M.J.

Published in:
Europace

DOI:
10.1093/europace/eut072

Publication date:
2013

Document Version
Publisher's PDF, also known as Version of record

Europace (2013) **15**, 1468–1474
doi:10.1093/europace/eut072

Comorbidity burden is associated with poor psychological well-being and physical health status in patients with an implantable cardioverter-defibrillator

Madelein T. Hoogwegt[1,2], Nina Kupper[1], Luc Jordaens[2], Susanne S. Pedersen,[1,2,3], and Dominic A.M.J. Theuns[2]*

[1]CoRPS – Department of Medical and Clinical Psychology, Tilburg University, PO Box 90153, 5000 LE, Tilburg, The Netherlands; [2]Department of Cardiology, Erasmus Medical Center, Room Bd416, PO Box 2040, 3000 CA, Rotterdam, The Netherlands; and [3]Department of Cardiology, Odense University Hospital, & Institute of Psychology, University of Southern Denmark, Odense, Denmark

Received 11 October 2012; accepted after revision 5 March 2013; online publish-ahead-of-print 21 April 2013

Aims Comorbidity burden has been linked to survival in patients with an implantable cardioverter-defibrillator (ICD), but no study has examined the influence on psychological well-being and health status. We examined the relationship between comorbidity burden and anxiety, depression, and health status in patients with an ICD during the first 12 months post-implantation using a prospective study design.

Methods and results Consecutively, implanted ICD patients ($N = 401$; 78% men) completed the Hospital Anxiety and Depression Scale and the Short Form Health Survey 36 (SF-36) at baseline, 3, 6, and 12 months post-implantation. Data were analysed using general linear mixed modelling repeated measures multivariable analysis of variance. The mean Charlson comorbidity index score was 3.5 ($\pm$ 2.4). In adjusted analyses, comorbidity burden was significantly associated with depression ($P = 0.003$) and the physical health status domains of the SF-36 (Physical Functioning: $P < 0.001$; Role Limitations—Physical: $P = 0.023$; Bodily Pain: $P = 0.004$; and General Health: $P = 0.025$) but not with anxiety ($P = 0.62$) and the mental health status domains of the SF-36 (all P's > 0.05). Chronic heart failure, chronic obstructive pulmonary disease, cerebrovascular disease, and renal failure were the comorbidities with the most impact on depression and physical health status.

Conclusion Comorbidity burden was a significant predictor of poorer psychological well-being and physical health status in ICD patients during the first 12 months post-implantation. In the care and management of ICD patients, it is important to recognize the impact of comorbidity burden on patients' mood and health status, and that adjunctive intervention may be warranted to enhance well-being.

Keywords Implantable cardioverter-defibrillator • Comorbidities • Depression • Anxiety • Health status

Introduction

The implantable cardioverter-defibrillator (ICD) is the first-choice therapy for patients at risk for sudden cardiac death due to ventricular arrhythmias.[1,2] Despite the effectiveness of ICD therapy demonstrated in clinical trials, patients enrolled in clinical trials do not fully reflect ICD patients seen in the real-world clinical setting, due to the former being younger and having less comorbidities.[3]

The presence of multiple comorbid conditions is associated with a poorer survival.[4–6] As a result of poorer physical functioning and increased problems in daily life, a higher number of comorbidities may also influence patients' psychological well-being, including symptoms of anxiety and depression, and health status.[6–8]

* Corresponding author. Tel: +31 10 703 2938; fax: +31 10 703 4420, Email: d.theuns@erasmusmc.nl

What's new?

- The impact of comorbidities on psychological well-being and health status in patients with an implantable cardioverter-defibrillator (ICD) has not yet been investigated, as the main focus has previously been the impact of the ICD itself in relation to psychological well-being.
- Implantable cardioverter-defibrillator patients comprise a heterogeneous group at increased risk of having multiple co-morbid conditions. As a result of heterogeneous presentation, detection of psychological distress is more difficult and these patients are at increased risk of not receiving the psychological care they need.
- The use of general linear mixed modelling analysis, a powerful statistical technique to analyse the data, reducing non-response bias and increasing statistical power.

Monitoring psychological status of patients with multiple comorbidities is thus of utmost importance, in particular because the variability in clinical presentation and types of comorbidities present may hinder the detection of psychological distress.[9] To our knowledge, no previous study has examined the impact of comorbidities on the well-being and health status of ICD patients but rather tend to have focused on the impact of ICD therapy. In addition, as the population of ICD patients is very heterogeneous with patients receiving implantation for a wide range of indications, the risk of an increased comorbidity burden is high.

The purpose of the current study was to examine the association between patients' pre-implantation Charlson comorbidity index (CCI) score, and anxiety, depression, and health status in patients with an ICD during the first 12 months post-implantation using a prospective study design.

Methods

Patients and study design

Between August 2003 and February 2010, 448 consecutive patients who were implanted with a first-time ICD in the Erasmus Medical Center, Rotterdam, The Netherlands, were enrolled in the *M*ood and personality as precipitants of arrhythmia in patients with an *I*mplantable cardioverter *D*efibrillator: *A* prospective *S*tudy (MIDAS). Patients with a life-expectancy of <1 year, being on the waiting list for heart transplantation, a history of psychiatric illness other than affective/anxiety disorders, or insufficient knowledge of the Dutch language, were excluded.

The study protocol was approved by the Medical Ethics Committee of the Erasmus Medical Center, and the study was conducted according to the Helsinki Declaration. An ICD nurse provided written and oral information on the study prior to ICD implantation. After obtaining written informed consent, patients were asked to complete a set of standardized and validated questionnaires at baseline (i.e. 1 day prior to implantation), and at 3, 6, and 12 months post-implantation. Information on baseline demographics and clinical characteristics was extracted from patients' medical records and purpose-designed questions in the questionnaires.

Measures

Comorbidities and the Charlson comorbidity index

Information on comorbidities prior to ICD implantation was obtained via chart abstraction from the patients' medical records and laboratory values at baseline. Renal functioning was assessed by estimating the baseline glomerular filtration rate (eGFR), according to the abbreviated Modification of Diet in Renal Disease (MDRD) Study equation.[10] In accordance with practice guidelines, an eGFR <60 mL/min/1.73 m^2 was considered as impaired renal functioning.[11] An abbreviated CCI score was composed with the following comorbid conditions: myocardial infarction (MI), congestive heart failure, cerebrovascular disease, chronic obstructive pulmonary disease, diabetes mellitus, peripheral vascular disease, renal failure, and any malignancy excluding metastatic tumours.[5] In order to obtain a comorbidity index that is in accordance with the original CCI, a weight of 2 was assigned to renal failure and any malignancy, and a weight of 1 to the other comorbid conditions.[12] By adding up the values assigned to each comorbid condition, a co-morbidity score was calculated for each patient. Because age is a risk factor for mortality independent of the presence of comorbid conditions and the incidence of comorbidities increased with higher age in our sample, we adjusted the score by adding one point to the score for each decade of life over the age of 50 years at the time of study entry, according to the validated combined comorbidity index.[5,13] The advantage of this abbreviated index is that it reckons with the co-morbid disorders most prevalent in and relevant to cardiac patients, and that age is included as an additional indicator of health.

Psychological well-being and health status

Symptoms of anxiety and depression were measured at baseline, and at 3, 6, and 12 months follow-up using the Hospital Anxiety and Depression Scale (HADS).[14] The HADS consists of seven items measuring symptoms of anxiety (HADS-A) and seven items measuring symptoms of depression (HADS-D), all scored on a 4-point Likert scale.[14] Scores range from 0 to 3 (total score range of 0–21), with higher scores reflecting more symptoms.[14] The HADS has good psychometric properties.[15]

The Short Form Health Survey 36 (SF-36) was used to assess patients' health status at baseline, and at 3, 6, and 12 months post-implantation.[16] The items contribute to eight subscales: Physical functioning, Role Limitations—Physical, Bodily Pain, Social Functioning, Mental Health, Role Limitations—Emotional, Vitality and General Health. Scores on the individual subscales range from 0 to 100, with higher scores indicating better health status, and a higher score on the Bodily Pain subscale indicating the absence of pain.[17] Psychometric properties for the SF-36 are adequate.[16]

Type D personality is the combined tendency to experience increased negative affectivity and social inhibition. The 14-item Type D scale (DS14), consisting of seven items measuring negative affectivity (i.e. 'I often feel unhappy') and seven items measuring social inhibition (i.e. 'I am a closed kind of person'), was used to assess Type D personality at baseline.[18] All items are scored on a 5-point Likert scale, ranging from 0 (false) to 4 (true), with a total score ranging from 0 to 28.[18] A cut-off score of ≥ 10 on both subscales defines individuals with a Type D personality.[19]

Statistical analyses

Repeated measures multivariable analysis of variance using general linear mixed modelling analysis was performed to test the longitudinal association between CCI and psychological well-being. This technique uses the data efficiently by also including incomplete cases in analyses.

Table 1 Baseline characteristics of the study sample[a]

	Total study population (*N* = 401)
Demographics	
Mean age (± SD)	58.4 (12.2)
Men	314 (78.3)
Single/no partner	26 (6.5)
Low education[b]	231 (57.6)
Clinical risk factors	
Primary prevention indication	265 (66.1)
CRT	112 (27.9)
Shocks during follow-up[c]	58 (14.5)
LVEF ≤35%[d]	300 (74.8)
Mean QRS (ms) (± SD)	130.3 (36.2)
CAD	231 (57.6)
Previous PCI	105 (26.2)
Previous CABG	83 (20.7)
Atrial fibrillation	91 (22.7)
Smoking	44 (11.0)
Medication use	
Amiodarone	74 (18.5)
Beta-blockers	320 (79.8)
Diuretics	229 (57.1)
ACE inhibitors	288 (71.8)
Statins	237 (59.1)
Digoxin	63 (15.7)
Psychological treatment[e]	77 (19.2)

ACE, angiotensin-converting enzyme; CABG, coronary artery bypass graft surgery; CAD, coronary artery disease; CRT, cardiac resynchronization therapy; LVEF, left ventricular ejection fraction; MI, myocardial infarction; *N*, number; PCI, percutaneous coronary intervention; QRS, QRS duration; SD, standard deviation.
[a]Results are presented as *N* (%), unless otherwise indicated.
[b]Education ≤13 years.
[c]Both appropriate (*N* = 44; 11.0%) and inappropriate (*N* = 16; 4.0%) shocks.
[d]Fifty-three of 401 (13.2% missing).
[e]Both psychotropic medication and treatment by a psychologist.

As a result of this, bias is limited and statistical power is preserved. First, intra-class correlations, a measure of score dependencies within patients, were computed for anxiety, depression and each of the SF-36 subscales. First, the CCI was tested as an associate of psychological well-being and health status over time; secondly, we assessed which individual comorbidities mainly accounted for the association between CCI and psychological well-being and health status.

A priori, we adjusted for gender, educational level, indication for ICD therapy, the presence of cardiac resynchronization therapy (CRT), ICD shocks, atrial fibrillation, smoking, the use of amiodarone, beta-blockers, and diuretics, the presence of psychological treatment, and Type D personality in multivariable analyses. All independent variables were defined as fixed variables (i.e. not varying over time). Analyses were performed using PASW Statistics 19 statistical software (PASW IBM Corp). For all tests, a $P < 0.05$ was considered to be statistically significant. The described effects in the 'Results' section are the relationship of CCI *at any time point* with the level of anxiety and depression symptoms, and health status over time, including all measurement occasions.

Results

Baseline characteristics

Of the 448 patients, 18 had missing data on one or more psychological measures. Twenty-nine patients had additional missing data on one or more clinical baseline characteristics. No systematic differences were found between patients included ($n = 401$) and patients excluded ($n = 47$) from analyses (all $P > 0.05$). The population was predominantly male (78%), with a mean age of 58 ± 12 years. Baseline characteristics of the study population are presented in *Table 1*. The prevalence of comorbid conditions included in the CCI is displayed in *Figure 1*. The most common non-cardiac comorbid conditions were renal failure, diabetes mellitus, and cerebrovascular disease. The number of comorbid conditions in patients varied from 0 to 6, with 25% of the patients having ≥3 comorbid conditions. Nineteen per cent of the patients had ≥2 non-cardiac comorbidities. Charlson comorbidity index scores ranged from 0 to 10, with the mean CCI score being 3.5 ± 2.4. In the

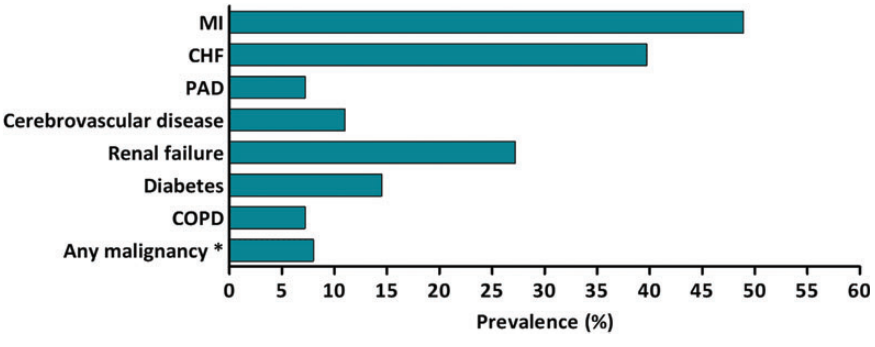

Figure 1 Prevalence (%) of the different comorbid conditions in the total study population. *Excluding metastatic tumours. CHF, chronic heart failure; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; PAD, peripheral arterial disease.

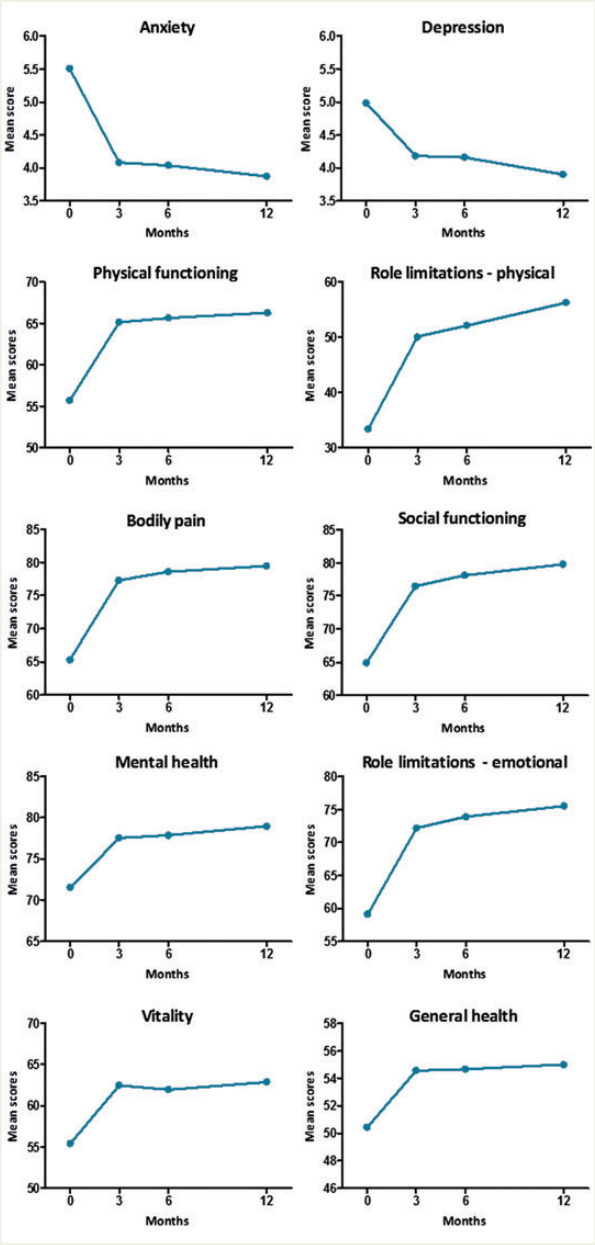

Figure 2 Mean scores of anxiety, depression, and health status during the 12 months post-implantation.

12 months period post-implantation, 15% of the patients received a shock, of which 4% was inappropriate.

Charlson comorbidity index as a determinant of psychological well-being and health status

Figure 2 depicts mean scores for anxiety, depression, and health status during the 12-month follow-up period. First, intra-class correlations were computed as a measure of correlation between the different measurement occasions (i.e. baseline, 3, 6, and 12 months follow-up). The consecutive measurements of anxiety and depression both showed an intra-class correlation of 0.30. With regard to health status, intra-class correlations varied from 0.37 to 0.73 for Role Limitations—Emotional and General Health, respectively, indicating a moderate to high correlation between the measurement moments, supporting the use of this specific repeated measures technique.

In *Table 2*, the results of the mixed modelling analyses are expressed as estimates, 95% confidence intervals (CIs), *t*- and *P*-values. A higher CCI prior to implantation was associated with more symptoms of depression over the follow-up period ($P = 0.003$). No association was found between CCI and anxiety. In multivariable analyses, the CCI remained as a significant predictor of depressive symptoms at any time point ($P = 0.003$) (*Table 2*).

With respect to the health status, in univariable analyses, a higher CCI prior to implantation was associated with poorer physical health status over the follow-up period, in terms of Physical Functioning ($P < 0.001$), Role Limitations—Physical ($P < 0.001$), more Bodily Pain ($P = 0.002$), poorer Role Limitations—Emotional ($P = 0.026$), Vitality ($P = 0.010$), and General Health ($P < 0.001$). In multivariable analyses, the association between CCI and health status remained significant for Physical Functioning ($P < 0.001$), Role Limitations—Physical ($P = 0.023$), Bodily Pain ($P = 0.004$), and General Health ($P = 0.025$) (*Table 2*).

The individual components of the Charlson comorbidity index as determinants of psychological well-being and health status

Subsequently, we investigated whether specific comorbidities included in the CCI accounted for the significant effects on psychological well-being and health status as displayed in *Table 2*. Chronic heart failure, chronic obstructive pulmonary disease, cerebrovascular disease, and renal failure were the most important predictors of depression and impaired health status (for all subscales, shown in *Table 3*). No individual effect of the different comorbidities was found on symptoms of anxiety. In multivariable analyses, when all comorbidities were entered in the model simultaneously, chronic heart failure, chronic obstructive pulmonary disease, cerebrovascular disease, and renal failure remained the most important predictors. Additionally, although age alone did not strongly predict psychological well-being and health status, it was an important determinant when all comorbidities were combined into one model.

Discussion

To our knowledge, this is the first study in ICD patients to examine the influence of comorbidity burden on psychological well-being and health status. We found that patient's comorbidity burden was an important predictor of psychological well-being and health status over the 12 months post-implantation. Having a higher comorbidity burden was associated with more symptoms of depression, but not anxiety, and with poorer physical functioning, more physical role limitations, more bodily pain and a poorer general health. Importantly, this association was present independent of the patient's pre-implantation personality profile, which has also shown to be an important predictor of anxiety, depression, and health status in patients with an ICD.[20] Our results

Table 2 Charlson comorbidity index as a determinant of anxiety, depression, and health status (adjusted analysis)[a]

	Estimate	95% CI	t	P
Anxiety	−0.06	[−0.19 to 0.08]	−0.84	0.40
Depression	0.21	[0.07 to 0.35]	2.95	0.003
SF-36 subscales				
Physical Functioning	−2.57	[−3.57 to −1.58]	−5.08	<0.001
Role Limitations—Physical	−1.67	[−3.10 to −0.23]	−2.29	0.023
Bodily Pain	−1.31	[−2.19 to −0.43]	−2.92	0.004
Social Functioning	−0.36	[−1.20 to 0.49]	−0.83	0.41
Mental Health	−0.19	[−0.80 to 0.43]	−0.60	0.55
Role Limitations— Emotional	−1.05	[−2.32 to 0.22]	−1.62	0.11
Vitality	−0.64	[−1.41 to 0.13]	−1.64	0.10
General Health	−0.97	[−1.82 to −0.12]	−2.25	0.025

[a]Adjusted for gender, educational level, indication for ICD therapy, CRT, the occurrence of shocks (both appropriate and inappropriate) during the 12 months post-implantation, atrial fibrillation, smoking, the use of amiodarone, beta-blockers, and diuretics, the presence of psychological treatment, and Type D personality.

correspond in part to findings of previous studies in the general older population[6,7] and in patients with acute MI,[8] where a higher comorbidity burden was found to be associated with more depressive symptoms and functional impairment. In patients with CRT, who also comprise an important group in our sample, the relationship between comorbidities and psychological well-being has not been investigated yet. However, as the course of health status in patients with CRT is comparable with the course of health status found in our study,[21,22] we expect that patients with CRT show a similar association between comorbidity burden and psychological well-being as patients with a defibrillator only.

We found no association between comorbidity score and anxiety. Around 25% of ICD patients report increased levels of anxiety.[20,23] However, the type of impairments in patients with multiple comorbidities might more easily induce symptoms of depression, by interfering with the patient's physical activity level, sleeping pattern, and social relationships, which in turn may lead to feelings of hopelessness and guilt.[6,8] This pattern corresponds more with depressive rather than anxious symptomatology.

No association was found between CCI score and mental health status. One would probably expect that in case of a positive association between CCI score and depressive symptoms, an association between CCI score and mental health status would also be present. However, the mental health status subscales of the SF-36, as used in the current study, may be too generally formulated and do not measure specific psychological problems, including symptoms of anxiety and depression. In addition, the mental health subscale has shown to lack sensitivity to measure changes in mental health.[24]

Chronic heart failure, chronic obstructive pulmonary disease, cerebrovascular disease, and renal failure were the most important associates of depressive symptoms and poorer health status. These comorbidities have both a worse short-term and long-term prognosis when compared with the other comorbidities. In addition, these patients may experience more restrictions both in physical and mental functioning. Their adverse impact on psychological well-being and health status is illustrated in our study. Cancer did not seem to have an influence on health status and symptoms of anxiety and depression in our patient group. However, as patients were asked to report on lifetime presence of cancer, a time span between the actual presence of cancer and the assessment of psychological problems could account for the absence of the relationship.

The finding that comorbid conditions are associated with poorer well-being and impaired health status is important for clinical practice. The variability in clinical presentation makes it difficult for physicians to detect psychological distress.[9] Physicians might attribute patients' psychological symptoms to their comorbidities rather than to psychological difficulties. However, it remains an important issue to focus on in daily practice, as both health status and depression have shown to be independent predictors of health care utilization in heart failure patients.[25,26] In addition, previous studies have shown that patients with comorbidities respond less well to psychological therapy than patients without such comorbidities.[27,28]

The limitations of this study should be acknowledged. First, it would have been interesting to investigate whether changes in CCI scores over time were predictive of psychological status during follow-up. However, information on comorbidities was only available at baseline. In addition, information on psychological well-being was based on self-report measures instead of clinical diagnoses according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR). However, minor depressive symptoms have also been associated with functional decline and mortality in cardiac patients.[29,30] Finally, the relatively short follow-up period does not allow drawing conclusions on the long-term relationship between CCI scores and psychological status.

This study also has important strengths. Research on the relationship between comorbid conditions and psychological functioning has mainly been focusing on symptoms of depression, while the influence on symptoms of anxiety and general daily functioning has been largely ignored. Furthermore, we used a powerful statistical

Table 3 Individual comorbidities from the Charlson comorbidity index as predictors of psychological well-being and health status

Psychological measures	Age		Renal failure		MI		CHF		DM		PAD		CVA/TIA		Chronic obstructive pulmonary disease		Cancer	
HADS	e	P	e	P	e	P	e	P	e	P	e	P	e	P	e	P	e	P
Anxiety	−0.32	0.06*	0.05	0.89	0.14	0.68	0.02	0.95	0.49	0.32	−0.40	0.55	0.87	0.12	1.18	0.08	−0.62	0.33
Depression	0.23	0.20	1.09	0.006	0.51	0.15	0.79	0.030	0.58	0.25	1.10	0.11	1.09	0.06	1.52	0.026	−0.21	0.75
SF-36																		
PF	−2.76	0.016	−12.32	<0.001*	−2.69	0.25	−14.03	<0.001‡	−9.49	0.004	−7.95	0.08	−13.25	<0.001†	−21.13	<0.001‡	−5.38	0.21
RL-P	−2.78	0.08	−9.65	0.009	−1.18	0.72	−15.93	<0.001‡	−9.40	0.044	−4.52	0.47	−10.19	0.06	−20.93	0.001*	−4.28	0.48
BP	−1.76	0.07	−2.97	0.19	−2.58	0.20	−4.94	0.015	−7.81	0.006*	−11.0	0.004*	−9.76	0.003*	−7.45	0.049	−0.33	0.93
SF	0.99	0.32*	−3.89	0.09	−1.62	0.42	−7.44	<0.001†	−5.20	0.07	−4.72	0.22	−7.09	0.031	−13.95	<0.001†	2.60	0.48
MH	0.95	0.22*	−2.20	0.21	−1.30	0.41	−1.70	0.29	−1.98	0.38	−3.19	0.29	−3.95	0.12	−6.40	0.033	2.82	0.33
RL-E	−1.71	0.25	−6.31	0.06	−7.84	0.008*	−3.67	0.23	−7.27	0.09	−0.71	0.90	−6.39	0.19	−5.60	0.33	5.88	0.28
VT	0.36	0.69	−5.66	0.006	1.20	0.52	−8.51	<0.001†	−2.22	0.40	−4.74	0.18	−7.50	0.012*	−9.81	0.005*	−0.49	0.89
GH	0.15	0.88*	−8.90	<0.001*	−2.15	0.28	−12.59	<0.001‡	−6.76	0.016	−4.30	0.26	−7.92	0.012	−11.78	0.002*	−2.09	0.57

BP, Bodily Pain; CHF, chronic heart failure; CVA, cerebrovascular accident; DM, diabetes mellitus; e, estimate; GH, General Health; MH, Mental Health; MI, myocardial infarction; PAD, peripheral arterial disease; PF, Physical Functioning; PROs, patient-reported outcomes; RL-E, Role Limitations—Emotional; RL-P, Role Limitations—Physical; SF, Social Functioning; SF-36, Short Form Health Survey 36; TIA, transient ischaemic attack; VT, Vitality.

*Significant on a $P < 0.05$ level in multivariable analyses (all comorbidities together in one model).

†Significant on a $P < 0.01$ level in multivariable analyses.

‡Significant on a $P < 0.001$ level in multivariable analyses.

technique to analyse the data, reducing non-response bias and increasing statistical power.

In conclusion, we found that patients with a higher comorbidity score reported more symptoms of depression and poorer health status on several domains. As the variability in clinical presentation of patients with comorbid conditions may hinder physicians from detecting psychological distress and referring the patient to adequate, tailor-made psychological care, in case of comorbidities, clinicians should be vigilant of the possibility that patients' psychological well-being and health status is at higher risk of being affected.

Acknowledgements

We would like to thank Agnes Muskens-Heemskerk for inclusion of the patients into the study and Simone Traa, Martha van den Berg, and Belinda de Lange for their help with data management.

Conflict of interest: L.J. has received research support from Biotronik, Boston Scientific, Medtronic, Sorin, and St Jude Medical. S.S.P. has received moderate consultancy and speaker's fees from St Jude Medical, Sanofi-Aventis, Medtronic, and Cameron Health BV. D.A.M.J.T. has received research support from Biotronik, Boston Scientific, St Jude Medical; he serves as a consultant for Cameron Health. The other authors report no disclosures.

Funding

This research was supported with a VENI (451-05-001) from the Netherlands Organisation for Scientific Research (NWO) and a VIDI (91710393) grant from the Netherlands Organisation for Health Research and Development (ZonMw), The Hague, The Netherlands to S.S.P.

References

1. Bardy GH, Lee KL, Mark DB, Poole JE, Packer DL, Boineau R *et al.* Amiodarone or an implantable cardioverter–defibrillator for congestive heart failure. *N Engl J Med* 2005;**352**:225–37.
2. The Antiarrhythmics versus Implantable Defibrillators (AVID) Investigators. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. *N Engl J Med* 1997; **337**:1576–84.
3. Scott PA, Sterns LD, Tang AS. Do patients at high risk of nonsudden cardiac death benefit from prophylactic ICD therapy? *Curr Opin Cardiol* 2012;**27**:1–7.
4. Lee DS, Tu JV, Austin PC, Dorian P, Yee R, Chong A *et al.* Effect of cardiac and noncardiac conditions on survival after defibrillator implantation. *J Am Coll Cardiol* 2007;**49**:2408–15.
5. Theuns DAMJ, Schaer BA, Soliman OII, Altmann D, Sticherling C, Geleijnse ML *et al.* The prognosis of implantable defibrillator patients treated with cardiac resynchronization therapy: comorbidity burden as predictor of mortality. *Europace* 2011;**13**:62–9.
6. Leong IY, Farrell MJ, Helme RD, Gibson SJ. The relationship between medical comorbidity and self-rated pain, mood disturbance, and function in older people with chronic pain. *J Gerontol A Biol Sci Med Sci* 2007;**62**:550–5.
7. Covinsky KE, Kahana E, Chin MH, Palmer RM, Fortinsky RH, Landefeld CS. Depressive symptoms and 3-year mortality in older hospitalized medical patients. *Ann Intern Med* 1999;**130**:563–9.
8. Watkins LL, Schneiderman N, Blumenthal JA, Sheps DS, Catellier D, Taylor CB *et al.* Cognitive and somatic symptoms of depression are associated with medical comorbidity in patients after acute myocardial infarction. *Am Heart J* 2003;**146**:48–54.
9. Docherty JP. Barriers to the diagnosis of depression in primary care. *J Clin Psychiatry* 1997;**58**:5–10.
10. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med* 1999;**130**:461–70.
11. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis* 2002; **39**:S1–S266.
12. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;**40**:373–83.
13. Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *J Clin Epidemiol* 1994;**47**:1245–51.
14. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983;**67**:361–70.
15. Spinhoven P, Ormel J, Sloekers PP, Kempen GI, Speckens AE, Van Hemert AM. A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. *Psychol Med* 1997;**27**:363–70.
16. Aaronson NK, Muller M, Cohen PDA, Essink-Bot M-L, Fekkes M, Sanderman R *et al.* Translation, validation, and norming of the Dutch language version of the SF-36 Health Survey in community and chronic disease populations. *J Clin Epidemiol* 1998;**51**:1055–68.
17. Ware J, Kosinski M. Interpreting SF-36 summary health measures: a response. *Qual Life Res* 2001;**10**:405–13.
18. Denollet J. DS14: Standard assessment of negative affectivity, social inhibition, and type D personality. *Psychosom Med* 2005;**67**:89–97.
19. Emons WHM, Meijer RR, Denollet J. Negative affectivity and social inhibition in cardiovascular disease: evaluating type-D personality and its assessment using item response theory. *J Psychosom Res* 2007;**63**:27–39.
20. Pedersen SS, Hoogwegt MT, Jordaens L, Theuns DAMJ. Pre implantation psychological functioning preserved in majority of implantable cardioverter-defibrillator patients. *Int J Cardiol* 2011;doi:10.1016/j.ijcard.2011.10.092
21. Versteeg H, van den Broek KC, Theuns DAMJ, Mommersteeg PM, Alings M, van der Voort PH *et al.* Effect of cardiac resynchronization therapy-defibrillator implantation on health status in patients with mild versus moderate symptoms of heart failure. *Am J Cardiol* 2011;**108**:1155–9.
22. Hoth KF, Nash J, Poppas A, Ellison KE, Paul RH, Cohen RA. Effects of cardiac resynchronization therapy on health-related quality of life in older adults with heart failure. *Clin Interv Aging* 2008;**3**:553–60.
23. Pedersen SS, Theuns DAMJ, Jordaens L, Kupper N. Course of anxiety and device-related concerns in implantable cardioverter defibrillator patients the first year post implantation. *Europace* 2010;**12**:1119–26.
24. Bech P, Olsen LR, Kjoller M, Rasmussen NK. Measuring well-being rather than the absence of distress symptoms: a comparison of the SF-36 Mental Health subscale and the WHO-Five Well-Being Scale. *Int J Methods Psychiatr Res* 2003;**12**:85–91.
25. Chan PS, Soto G, Jones PG, Nallamothu BK, Zhang Z, Weintraub WS *et al.* Patient health status and costs in heart failure. *Circulation* 2009;**119**:398–407.
26. Sullivan M, Simon G, Spertus J, Russo J. Depression-related costs in heart failure care. *Arch Intern Med* 2002;**162**:1860–6.
27. Schultz SK. Depression in the older adult: the challenge of medical comorbidity. *Am J Psychiatry* 2007;**164**:847–8.
28. Pohle K, Domschke K, Roehrs T, Arolt VB, Baune BT. Medical comorbidity affects antidepressant treatment response in patients with melancholic depression. *Psychother Psychosom* 2009;**78**:359–63.
29. Penninx BWJH, Beekman ATF, Honig A, Deeg DJH, Schoevers RA, van Eijk JTM *et al.* Depression and cardiac mortality: results from a community-based longitudinal study. *Arch Gen Psychiatry* 2001;**58**:221–7.
30. Vaccarino V, Kasl SV, Abramson J, Krumholz HM. Depressive symptoms and risk of functional decline and death in patients with heart failure. *J Am Coll Cardiol* 2001; **38**:199–205.